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Starting from readily available pyroglutamic esters **1**, some new 1,3,4-oxadiazole-2-thione derivatives, bonded to a pyrrolidinone ring were synthesised and characterised by their spectral data.

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1,3,4-Oxadiazole-2-thione derivatives are reported to show a broad spectrum of biological activities [1]. Some of these compounds have been shown to exhibit bactericide and fungicide properties [2]. It is also reported in the literature that some 1,3,4-thiadiazole bonded to the nitrogen of a lactam type heterocycle possess phytosanitary activity [3]. These observations, and our interest in pyroglutamic acid chemistry [4], prompted us to realise the synthesis of an, as yet, unreported series of 1,3,4-oxadiazolethione derivatives bonded to a lactam ring with possible fungicide and herbicidal properties.

The starting materials 5-(5-oxo-2-pyrrolidinyl)-1,3,4-oxadiazole-2-thiones **3** were prepared [5] by reaction of the pyroglutamic hydrazides **2** with potassium hydroxyde and carbon disulfide under reflux in ethanol, followed by the acidification with dilute hydrochloric acid. The pyroglutamic hydrazides **2** were prepared [6] by reaction of hydrazine hydrate and pyroglutamic esters **1** in methanol under reflux for 90 hours. The hydrazide **2** (R = H) and the ester **1** (R = CH₂ Ph) were previously described [7,8].

The thioethers **4** were prepared [9] by reaction of thiones **3** and appropriate alkyl halides in sodium hydroxyde. The sulfone **5** was prepared [10] by reaction of thione **3** (R = CH₂ Ph, R' = Me) with potassium permanganate in aqueous acetic acid. The physical properties and yields for new compounds are given in Table 1.

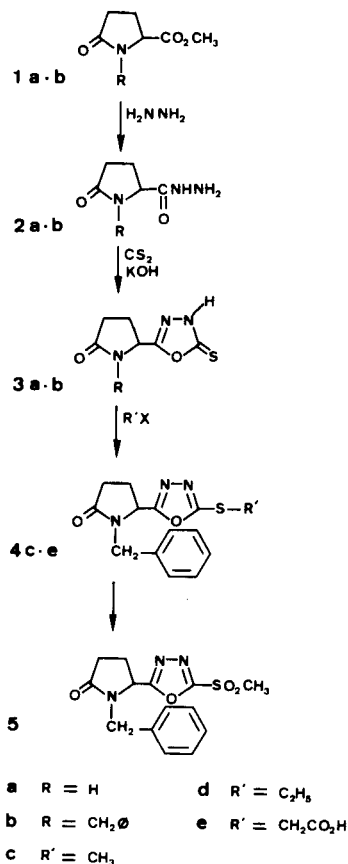


Table 1

Physical Data of New Compounds

Compound No.	R	R'	Yield %	MP, °C	Molecular Formulae	C	Microanalyses			Calculated			
							Found H	Found N	Found S	Calculated C	Calculated H	Calculated N	Calculated S
2b	CH ₂ Ph		82	120	C ₁₂ H ₁₅ N ₃ O ₂	62.00	6.49	17.87		61.79	6.48	18.01	
3a	H		77	238	C ₆ H ₇ N ₃ O ₂ S	38.66	3.78	22.31	17.23	38.91	3.81	22.69	17.32
3b	CH ₂ Ph		78	189	C ₁₃ H ₁₃ N ₃ O ₂ S	56.86	4.60	15.43	11.50	56.71	4.76	15.26	11.65
4c	CH ₂ Ph	CH ₃	83	62	C ₁₄ H ₁₅ N ₃ O ₂ S	57.87	5.32	14.31	10.97	58.11	5.23	14.52	11.08
4d	CH ₂ Ph	C ₂ H ₅	61	61	C ₁₅ H ₁₇ N ₃ O ₂ S	59.34	5.72	13.70	10.55	59.39	5.65	13.85	10.57
4e	CH ₂ Ph	CH ₂ CO ₂ H	45	135	C ₁₅ H ₁₅ N ₃ O ₄ S	54.04	4.54	12.60	9.62	53.87	4.66	12.85	9.93
5	CH ₂ Ph		51	125	C ₁₄ H ₁₅ N ₃ O ₄ S	52.36	4.50	12.98	9.99	52.32	4.71	13.08	9.98

Table 2

IR, UV and ¹H-NMR Spectral Data of New Compounds

Compound No.	IR (Nujol) cm ⁻¹	UV (MeOH) λ MAX (ε.10 ⁴)(nm)	¹ H NMR (Solvent) (ppm)
2b	3300 (NH), 1690, 1670 (C=O)	201 (1.8)	(Deuteriochloroform): 1.8-2.7 (m, 4H), 2.7-3.8 (s, broad, 2H) [a], 3.89 (d, J = 15 Hz, 1H), 3.80-4 (m, 1H), 5 (d, J = 15 Hz, 1H), 7.3 (s, 5H), 7.3-8.5 (s, broad, 1H) [a]
3a	3160 (NH), 1675 (C=O), 1640, 1620 (C=N), 1320 (C=S)	201 (0.8), 265 (1.6)	(Deuteriochloroform with 5% DMSO-d ₆): 2.2-2.7 (m, 4H), 3.7-4.3 (s, broad, 1H) [a], 4.6-5 (m, 1H), 8.04 (s, 1H) [a]
3b	1660(C=O), 1500 (C=N), 1350 (C=S)	204 (1.7), 266 (1.6)	(Deuteriochloroform with 10% DMSO-d ₆): 2.1-2.8 (m, 4H), 3.3-4.4 (s, broad, 1H) [a], 4.08 (d, J = 14.1 Hz, 1H), 4.4-4.8 (m, 1H), 4.83 (d, J = 14.1 Hz, 1H), 7.26 (s, 5H)
4c	1690(C=O), 1500, 1580 (C=C, C=N)	202 (1.8), 238 (0.8)	(Deuteriochloroform): 2-2.8 (m, 4H), 2.55 (s, 3H), 4.02 (d, J = 15 Hz, 1H), 4.65 (d, J = 15 Hz, 1H), 4.50-4.83 (m, 1H), 7.13 (s, 5H)
4d	1690 (C=O), 1500, 1590 (C=C, C=N)	202 (1.8), 238 (0.8)	(Deuteriochloroform): 1.42 (t, J = 7.5 Hz, 3H), 2-2.83 (m, 4H), 3.17 (q, J = 7.5 Hz, 2H), 4.08 (d, J = 15 Hz, 1H), 4.70 (d, J = 15 Hz, 1H), 4.60-4.85 (m, 1H), 7.23 (s, 5H)
4e	1725, 1670 (C=O), 1500 (C=C)	204 (2), 265 (0.8)	(Deuteriochloroform): 2.1-2.8 (m, 4H), 3.97 (s, 2H), 4.40 (d, J = 15 Hz, 1H), 4.59 (d, J = 15 Hz, 1H), 4.6-5.1 (m, 1H), 4.78 (s, 1H) [a], 7.18 (s, 5H)
5	1670 (C=O), 1500 (C=C), 1340-1150 (SO ₂)	204 (1.7)	(Deuteriochloroform): 2-2.85 (m, 4H), 3.35 (s, 3H), 4.28 (d, J = 15 Hz, 1H), 4.66 (d, J = 15 Hz, 1H), 4.73-4.94 (m, 1H), 7.17 (s, 5H)

[a] These peaks disappear upon addition of deuterium oxide.

All the newly synthesised compounds gave satisfactory spectral data, and the structures, particularly the position of the alkylations, were assigned on the result of the oxydation reaction and on the basis of elemental analysis, uv (methanol), ir (nujol) and ¹H nmr spectral data, given in Table 2.

The results of tests showed that most of the compounds prepared have a herbicidal activity; the best results were obtained with compound **4d** (0.5 g/l).

EXPERIMENTAL

Melting points are uncorrected. The ir spectra were recorded on a "Perkin Elmer 700" spectrometer, the nmr spectra on a "Hitachi Perkin Elmer R-600" at 60 MHz, using tetramethylsilane as an internal reference and the uv spectra on a "Beckman uv 5240" (10⁻⁴ mole.l⁻¹, in methanol). Elemental analyses were performed by the "Central Micro Analytical Departement" of CNRS in Thiais, France.

1-Benzylpyroglutamichydrazide (**2b**).

Methyl 1-benzylpyroglutamate [8] (80 g, 0.344 mole) was dissolved in methanol (80 ml) and hydrazine hydrate (28 g, 0.549 mole, 98%). The mixture was refluxed for 90 hours. The solid which separated after cooling was filtered, washed with cold methanol and dried, mp 119-120° (water), yield 82%.

1,3,4-Oxadiazole-2-thiones (**3a-b**).

A mixture of hydrazide **2a-b** (0.25 mole), potassium hydroxide (0.25 mole), carbon disulfide (38 g, 0.5 mole) and ethanol (400 ml) was heated under reflux for 48 hours. The excess solvent was removed by vacuum evaporation, and the residue was dissolved in water and acidified with acetic acid. The product was recrystallized from water (**3a**) or ethanol (**3b**).

2-Alkylthio-1,3,4-oxadiazoles (**4c-e**).

A mixture of thione **3** (0.05 mole), sodium hydroxide (0.05 mole for **4c-d**, 0.1 mole for **4e**) and the appropriate alkyl halide (0.06 mole) was stirred in 100 ml of water for 6 hours. The resulting thioether was col-

lected by filtration, washed with water, dried and recrystallized from suitable solvent.

5-(5-Oxo-1-benzyl-2-pyrrolidinyl)-2-methylsulfonyl-1,3,4-oxadiazole (**5**).

A solution of potassium permanganate (1.8 g, 0.014 mole) in water (5 ml) was dropped into a solution of thioether **4c** (2.9 g, 0.009 mole) in acetic acid (30 ml). After 20 minutes, the mixture was discoloured with sodium bisulfite and filtered. The resulting solution was extracted with dichloromethane. The organic solution was washed with sodium carbonate, dried, and the solvent was evaporated. The sulfone was recrystallized from methanol-ether. The yield was 51%.

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